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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,539	01/26/2004	Stephen J. Karlik	1002010-000854	9237

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EXAMINER	
HUYNH, CARLIC K	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
03/13/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/763,539	KARLIK ET AL.	
	Examiner	Art Unit	
	CARLIC K. HUYNH	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15-31,33,34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 15-21* is/are withdrawn from consideration.

5)☒ Claim(s) *13* is/are allowed.

6)☒ Claim(s) *1,2,5-12,22-31,33,34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *14 September 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on November 15, 2007 is acknowledged.

Status of the Claims

1. Claims 1-13, 15-31, 33-34, and 36-38 are pending in the application, with claims 14, 32, 35, and 39-91 are cancelled in an "Amendment – Non-Final Rejection" filed on November 15, 2007. Claims 3-4 and 15-21 are further withdrawn. Accordingly, claims 1-2, 5-12, 22-31, 33-34, and 36-38 are being examined on the merits herein.

Election/Restrictions

2. Applicant's election without traverse of Group I, originally claims 1-38, in the reply filed on February 15, 2007 is acknowledged.

3. Applicant's election without traverse of the species of (1) a compound of formula IC, where R^x is hydroxyl, as a species of a compound, (2) prednisolone as a species of an anti-inflammatory agent or immunosuppressant, and (3) multiple sclerosis as a species of a condition which demyelinates cells, in the reply filed on February 15, 2007 is acknowledged.

Claims 3-4, 15-21, 32 and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on February 15, 2007.

It is noted Applicants have cancelled claims 14, 32, 35, and 39-91 in an "Amendment – Non-Final Rejection" filed on November 15, 2007.

Accordingly, claims 1-2, 5-12, 22-31, 33-34, and 36-38 are being examined on the merits herein.

Claim 13 was found to be free of the prior art. Accordingly, the search was broadened to encompass the compounds of formula I, formula IA, and formula IB pursuant to M.P.E.P. § 803.02.

The objections to the Specification for use of trademarks have been withdrawn in view of Applicants' amendments.

The rejections under 35 U.S.C. 103 to claims 1-12, 15-31, 33-34, and 36-38 have been withdrawn in light of Applicants' arguments.

The Obviousness-Type Double Patenting Rejections have been withdrawn in light of Applicants' arguments. It is noted that the Obviousness-Type Double Patenting Rejections using US 2005/0272668 has been withdrawn because the patent application has been abandoned.

The following new grounds of rejections are necessitated because claims 3-4 and 15-21 were further withdrawn.

Information Disclosure Statement

The Information Disclosure Statement submitted on September 14, 2007 is acknowledged.

Claim Objections

4. Claims 23-31, 33-34, and 36-38 are objected to under 37 CFR 1.75(c) as being in improper form because they contain multiple dependency to claims 5, 13, and 15. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-2, 5-12, 22-31, 33-34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thorsett et al. (US 6,489,300) in view of Kawamura et al. (US 2002/0161006).

Thorsett et al. teach a method of treating multiple sclerosis comprising administering VLA-4 inhibitors to humans (abstract). The compounds taught are of formula I, which meets the limitations of the compounds of formula I, IA, and IB of the instant claims 1, 2, and 5, respectively (page 235, Formula I). The compound of formula I, namely N-(toluene-4-sulfonyl)-

L-prolyl-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine ethyl ester, meets the limitations of instant claim 22 (column 8, lines 36-37). The compounds are administered intravenously (page 136, line 5). For intravenous administration, the dose ranges from 20 μg to 500 μg per kilogram body weight (page 153, lines 14-16).

Thorsett et al. do not teach prednisolone.

Kawamura et al. teach a composition comprising of prednisolone and adhesion molecule inhibitors, e.g. VLA-4 antagonist, can be used for treating multiple sclerosis via parenteral administration in humans (page 1, paragraph [0001]; page 9, paragraph [0164]; page 12, paragraph [0200]; and page 23, paragraph [0305]).

To a person of skill in the art at the time of the invention, it would have been obvious to employ the VLA-4 inhibitors of Thorsett et al. to contain prednisolone because the compounds of Kawamura et al. contain prednisolone and according to Kawamura et al., compositions containing prednisolone has been used for treating multiple sclerosis.

The motivation to combine the compounds of Thorsett et al. to the compounds of Kawamura et al. is that the compounds of Kawamura et al. contain prednisolone, which has been used for treating multiple sclerosis.

It is noted that "It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose" and "It is obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose". *In re Kerkhoven*, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Regarding the method of promoting remyelination of nerve cells as recited in instant claims 1-38, the methods of Thorsett et al. and Kawamura et al. teach the methods for the treatment of multiple sclerosis. Thus the disease process is disclosed and treated. Multiple sclerosis is known in the art as a demyelinating condition. Any method used to treat multiple sclerosis would treat and stop the disease progression, which would then allow for remyelination of diseased nerve cells.

Regarding the chronic administration of the compound as recited in instant claims 27-28, Thorsett et al. teach administration of the compound through a transdermal delivery device to provide continuous infusion of the compounds in controlled amounts (page 143, lines 28-31). Since Thorsett et al. teach providing continuous infusion of the compounds, it would be obvious to one skilled in the art to chronically administer the compound using such a delivery device.

Regarding the administration results in an effective blood level of the compound of $\geq$ 10 ng/ml as recited in instant claim 37, Thorsett et al. teaches for intravenous administration, the dose ranges from 20 μg to 500 μg per kilogram body weight, which meets the limitations of the instant claims (page 153, lines 14-16). It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the quantity of the compound for intravenous administration provided in a composition, according to the guidance set forth in Thorsett et al., to provide the desired blood level of the compound following intravenous administration of the compound. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223, 235 (CCPA 1955).

Double Patenting

Obviousness-Type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-2 and 5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20 and 21 of Ashwell et al. (US 6,291,453), claims 13 and 14 of Thorsett et al. (US 6,362,341), claims 34 and 35 of Thorsett et al. (US 6,492,421), claims 1 and 4 of Yednock et al. (US 6,939,855), claims 12 and 13 of Thorsett et al. (US 7,030,114), claim 14 of Thorsett et al. (US 7,288,526), and claims 1, 2, and 20 of Thorsett et al. (US 7,320,960) in view of Thorsett et al. (US 6,489,300).

The instant claims are directed to a method of promoting remyelination of nerve cells comprising administering a compound of formula I, IA, or IB. It is noted that multiple sclerosis is known in the art as a demyelinating condition.

The claims of Ashwell et al. (US 6,291,453), Thorsett et al. (US 6,362,341), Thorsett et al. (US 6,492,421), Yednock et al. (US 6,939,855), Thorsett et al. (US 7,030,114), Thorsett et al. (US 7,288,526), and Thorsett et al. (US 7,320,960) are directed to a method of treating multiple sclerosis comprising administering compounds of formula I, which is identical to the instant compounds.

Regarding the method of promoting remyelination of nerve cells as recited in instant claims 1-38, the methods of Thorsett et al. (US 6,489,300) teach the methods for the treatment of multiple sclerosis. Thus the disease process is disclosed and treated. Multiple sclerosis is known in the art as a demyelinating condition. Any method used to treat multiple sclerosis would treat and stop the disease progression, which would then allow for remyelination of diseased nerve cells.

Conclusion

7. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

ckh